Replicating Impaired Resting State Functional Connectivity in Chronic Cocaine Users

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Introduction

Cocaine abuse has been associated with alterations in functional connectivity of the reward-related mesocorticolimbic circuit in the brain. However, neuroscientific findings are not as valuable unless they are replicable after repeated measurement, as only then can treatments be developed based on reliable biomarkers. The aim of this study was to assess the reliability of the findings of a previous resting-state functional magnetic resonance imaging (rsfMRI) study that compared functional connectivity differences in United States cocaine users (CU) and matched healthy controls (HC)[1].

Method

Resting-state fMRI data was obtained for 20 active CU (mean age 33 ± 7.39 SD, all males) and 20 matched HC of Mexican origin. All CU were educated at least up to middle school and belong to lower middle class. Subjects were assessed with a comprehensive history and physical examination, and a psychiatric interview assessing substance use among other things. Ten minute rsfMRI data was collected with 3 mm^3 voxels and a TR = 2 s. Subsequent seed-based functional connectivity analyses for seven bilateral seeds of 3 mm radius placed in the Nucleus Accumbens (NAcc), Amygdala, Hippocampus, Mediodorsal (MD) Thalamus, Rostral Anterior Cingulate Cortex (rACC), Ventral Tegmental Area (VTA) and Insular cortex followed by t-tests revealed group differences in connectivity patterns.

Results

Both the groups demonstrated similar network connections but reduced connectivity strength overall for CU for all seeds except NAcc. Reduced resting-state functional connectivity strength (rsFCs) was observed between the VTA seed and the thalamus and lentiform nucleus. Amygdala displayed the same effect with parts of prefrontal cortex, insula, PCC as in the original study with the addition here of substantia nigra. Hippocampus showed decreased rsFCs with prefrontal cortex, rostral and dorsal anterior cingulate cortex (ACC), several frontal regions and left caudate nucleus. Unlike the original study, rACC didn't show a direct relation with amygdala in our case but both amygdala and rACC relate to PCC (BA 23). Rostral ACC showed decreased rsFCs with temporal gyrus in addition to fusiform and lingual gyrus. Insula showed the same reduced effect with parts of prefrontal cortex and ACC. Reduced connectivity was reported between thalamus and major parts of cingulate cortex, thalamus and occipital gyrus.

Discussion

CU showed reduced rsFCs for a number of regions with a large part of the results in agreement with the original study. Overall, greater number of regions demonstrated

reduced connectivity with the seeds. A distinctive finding is the reduced rsFCs observed of NAcc seed with ACC/PCC and increased connectivity with frontal regions around Broca's area. The former finding was expected in the original study but was not found and the latter was not expected. However, increase in rsFCs of NAcc and Amygdala with frontal regions was observed in heroin addicts in a Chinese sample[2]. These differences question the reliability of findings of the original study and question the robustness of rsFCs as a metric to assess alterations in brain functioning. One explanation could be the characteristics of populations studied, in addition to limitation of smaller sample size.

References

1. Gu H, Salmeron BJ, Ross TJ, et al. Mesocorticolimbic Circuits are Impaired in Chronic Cocaine Users as Demonstrated by Resting State Functional Connectivity. NeuroImage. 2010; 53(2):593-601. doi:10.1016/j.neuroimage.2010.06.066.

2. Ma N et al., Addiction related alteration in resting-state brain connectivity, Neuroimage. 2010 Jan 1; 49(1):738-44. doi: 10.1016/j.neuroimage.2009.08.037